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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/058,546	04/10/1998	WALTER H. GUNZBURG	2316.1008-000	7592

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JENKINS, WILSON & TAYLOR, P. A.
3100 TOWER BLVD
SUITE 1400
DURHAM, NC 27707

EXAMINER	
WILSON, MICHAEL C	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 08/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/058,546	GUNZBURG ET AL.	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 June 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,9-11,13,14,19,26,27,31,33,36-40,43-45,48-50,53-55,65 and 66* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *44 and 49* is/are allowed.

6)☒ Claim(s) *1-4,9-11,13,14,19,26,27,31,33,36-40,43,45,48,50,53-55,65 and 66* is/are rejected.

7)☒ Claim(s) *1-4,9-11,13,14,19,26,27,31,33,36-40,43-45,48-50 and 53-55* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

5-0-0

DETAILED ACTION

Claims 5-8, 12, 15-18, 20-25, 28-30, 32, 34, 35, 41, 42, 46, 47, 51, 52 and 56-64 have been cancelled. Claims 65-66 have been added. Claims 1-4, 9-11, 13, 14, 19, 26, 27, 31, 33, 36-40, 43-45, 48-50, 53-55, 65 and 66 are pending and under consideration in the instant office action.

Applicant's arguments filed 6-1-05 have been fully considered but they are not persuasive.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Objections

Claim 1:

Claim 1 is objected to because the preamble is unclear, because the preamble does not correlate to the final method step of the claim and because the body of the claim includes extraneous information. Claim 1 is drawn to a method of producing a recombinant retroviral particle, said recombinant retroviral particle comprising an RNA sequence encoding an SDI-1 polypeptide or functional fragment thereof.

The preamble in claim 1 would be more clear written as a –method of producing a recombinant retroviral particle, said retroviral particle comprising an RNA sequence encoding a SDI-1 polypeptide or fragment thereof, the method comprising...--.

Step a) 1) would be more clear written as -- a nucleic acid sequence encoding an SDI-1 polypeptide or fragment thereof, wherein said SDI-1 polypeptide or fragment thereof inhibits cell proliferation...--. Step i) would require parallel language.

Step b) would be more clear as –producing a retroviral particle in the producer cell line, wherein said retroviral particle encodes said SDI-1 polypeptide or functional fragment thereof --.

Inclusion of the phrase "upon infection..." in i) under step b) is unclear because it appears to be another step relating to infecting target cells with the retroviral particle; however, the preamble of the claim states the method stops at the step of producing a retroviral particle encoding SDI-1. If the phrase is a functional limitation of the retroviral particle, the phrase must be written more clearly (see 112/2nd).

Use of items 1), 2) and 3) under step a) while listing items i) and ii) under step b) is confusing.

The phrase "encoding an SDI-1 polypeptide or a functional fragment thereof" in the preamble of claim 1 should parallel the description of the retroviral vector in item a) 2) which currently requires an SDI-1 coding sequence encoding an SDI-1 polypeptide or functional fragment thereof.

Claim 13:

The preamble in claim 13 would be more clear written as an --isolated producer cell line stably transfected with a retroviral vector encoding an SDI-1 polypeptide or a [functional] fragment thereof, said retroviral vector comprising in 5' to 3' order...--.

Item b) would be more clear written as -- a nucleic acid sequence encoding an SDI-1 polypeptide or fragment thereof, wherein said SDI-1 polypeptide or fragment thereof inhibits cell proliferation...--. Step i) would require parallel language.

Inclusion of the phrase "upon infection..." in i) under item c) is unclear because it does not relate to the retroviral particle produced by the producer cell line and appears to be a functional limitation of the retroviral particle. As written, the functional limitation of the retroviral particle is unclear (see 112/2nd).

Use of items a), b) and c) while listing items i) and ii) under step c) is confusing.

Claim 33:

The preamble in claim 33 would be more clear written as a –method of producing a recombinant retroviral particle comprising an RNA sequence encoding an SDI-1 that inhibits cell proliferation, the method comprising...--.

Item a) 2) would be more clear written as -- a nucleic acid sequence encoding an SDI-1 polypeptide that inhibits cell proliferation—to parallel the language in the preamble.

Inclusion of the phrase "upon infection..." in i) under step b) is unclear because it appears to be another step relating to infecting target cells with the retroviral particle; however, the preamble of the claim states the method stops at the step of producing a retroviral particle encoding SDI-1. If the phrase is a functional limitation of the retroviral particle, the phrase must be written more clearly.

Use of items 1), 2) and 3) under step a) while listing items i) and ii) under step b) is confusing.

Claim 39:

The preamble in claim 39 would be more clear written as an --isolated producer cell line stably transfected with a retroviral vector encoding an SDI-1 polypeptide that inhibits cell proliferation, said retroviral vector comprising in 5' to 3' order...--.

Item b) would be more clearly written as -- a nucleic acid sequence encoding an SDI-1 polypeptide that inhibits cell proliferation...--. Step i) would require parallel language.

Inclusion of the phrase "upon infection..." in i) under item c) is unclear because it does not relate to the retroviral particle produced by the producer cell line and appears to be a functional limitation of the retroviral particle. As written, the functional limitation of the retroviral particle is unclear (see 112/2nd).

Use of items a), b) and c) while listing items i) and ii) under step c) is confusing.

Claim 44:

Claim 44 would be clearer written as

A method of producing a recombinant retroviral particle comprising an RNA sequence encoding amino acids 1-71 of human SDI-1, the method comprising:

a) stably transfecting an isolated producer cell line with a retroviral vector comprising a DNA sequence encoding amino acids 1-71 of human SDI-1,

wherein:

i) amino acids 1-71 of human SDI-1 inhibit cell proliferation; and

ii) said producer cell line comprises at least one DNA construct encoding a protein required for retroviral packaging--.

Claim 45:

The preamble in claim 45 would be more clear written as an --isolated producer cell line stably transfected with a retroviral vector encoding amino acids 1-71 of human SDI-1, said retroviral vector comprising in 5' to 3' order...--.

Item b) would be more clear written as -- a nucleic acid sequence encoding amino acids 1-71 of human SDI-1, wherein said amino acids 1-71 of human SDI-1 inhibit cell proliferation...--. Step i) would require parallel language.

Inclusion of the phrase "upon infection..." in i) under item c) is unclear because it does not relate to the retroviral particle produced by the producer cell line and appears to be a functional limitation of the retroviral particle. As written, the functional limitation of the retroviral particle is unclear (see 112/2nd).

Use of items a), b) and c) while listing items i) and ii) under step c) is confusing.

Claim 49 would be clearer written as

A method of producing a recombinant retroviral particle comprising an RNA sequence encoding amino acids 42-58 of human SDI-1, the method comprising:

a) stably transfecting an isolated producer cell line with a retroviral vector comprising a DNA sequence encoding amino acids 42-58 of human SDI-1, wherein:

i) amino acids 42-58 of human SDI-1 inhibit cell proliferation; and

ii) said producer cell line comprises at least one DNA construct encoding a protein required for retroviral packaging--.

Claim 50:

The preamble in claim 50 would be more clear written as an --isolated producer cell line stably transfected with a retroviral vector encoding amino acids 42-58 of human SDI-1 polypeptide, said retroviral vector comprising in 5' to 3' order...--.

Item b) would be more clear written as -- a nucleic acid sequence encoding amino acids 42-58 of human SDI-1, wherein said amino acids 42-58 of human SDI-1 inhibit cell proliferation...--. Step i) would require parallel language.

Inclusion of the phrase "upon infection..." in i) under item c) is unclear because it does not relate to the retroviral particle produced by the producer cell line and appears to be a functional limitation of the retroviral particle. As written, the functional limitation of the retroviral particle is unclear (see 112/2nd).

Use of items a), b) and c) while listing items i) and ii) under step c) is confusing.

The objections regarding claims 14 and 21 have been withdrawn in view of the amendments.

The rejection of claims 21, 59 and 63 regarding the phrase "administering to the individual at a site of the tumor or the restenosis the capsule of claim 15" has been withdrawn because the claims have been canceled.

The objection of claims 27, 31 has been withdrawn in view of the amendment.

The objection of claim 63 regarding "or restenosis" has been withdrawn because the claim has been canceled.

Interview Summary

Applicants' summary of the interview of 5-5-05 is inaccurate. The rejections were discussed in general; possible arguments and possible amendments were discussed; no agreement was reached during the interview with respect to the new matter rejections or indefiniteness rejections as asserted by applicants. Please see the interview summary of 5-5-05. Applicants' comments under the "Telephone Interview Summary" on pg 13 of applicants' response filed 6-1-05 will not be considered as "arguments."

Claim Rejections - 35 USC ' 112

New Matter

The rejections of claims 1-4, 9-11, 13, 14, 19, 26, 27, 31, 33, 36-40, 43-45, 48-50 and 53-55 under 35 U.S.C. 112, first paragraph, new matter, have been withdrawn.

The phrase "in 5' to 3' order" has support in Fig. 7 and Example 3.

The rejection regarding the phrase "wherein said insertion comprises a polylinker sequence into which a regulatory element or a promoter has been cloned" has been withdrawn in view of the amendment and applicants' arguments.

The rejection regarding the phrase "after infection of a target cell... ...SDI-1 coding sequence in said target cell" has been withdrawn in view of applicants' arguments.

The rejection regarding the phrase "at a site of the tumor or restenosis" in claims 27 and 31 has been withdrawn in view of the amendment and applicants' arguments.

The rejection regarding the phrase "Whey Acidic protein... ...regulatory elements" in claim 37 has been withdrawn in view of applicants' arguments.

Enablement

The rejection of claims 15, 16, 20, 21, 23, 27, 31, 32, 41, 42, 46, 47, 51, 52, 56-59, 61 and 63 under 35 U.S.C. 112, first paragraph, enablement has been withdrawn in view of the amendment and applicants' argument.

The rejection of claims 15, 16, 20, 21, 23, 41, 42, 46, 47, 51, 52, 58, 59, 61 and 63 regarding capsules comprising producer cells that make retroviral particles encoding SDI-1, and methods of treating tumors or restenosis using the capsules has been withdrawn because the claims have been canceled.

The rejection regarding claims 21, 23, 27, 31, 59, 61 and 63 and the route of administration has been withdrawn because claims 21, 23, 59, 61 and 63 have been

canceled and because claims 27 and 31 are limited to administering into said tumor or a site of restenosis of said subject.

The rejection regarding "functional fragments" of SDI-1, specifically amino acids 1-71 of SDI-1, that inhibit cell proliferation has been withdrawn. Pg 8,lines 20-25, describe amino acids 1-71 of the SDI-1 as having essentially the same effect as full length SDI-1.

The rejection of claim 15, 46, 47, 51, 52 and 63 regarding using amino acids 42-58 of SDI-1 to inhibit cell proliferation is withdrawn because the claims have been canceled.

Claims 4 and 49 are directed toward making retroviral particles encoding amino acids 42-58 of the SDI-1 protein that inhibit cell proliferation. Support can be found on pg 8, line 22, of the specification, which states:

> The active domains of SDI-I are present within amino acids 1-71. Active domains also comprise amino acids 42 to 47, 53 to 58 and 66 to 71. Deletion of amino acids 53 to 58 was found to result in the greatest loss of DNA synthesis inhibitory activity (50% of full length DNA). Deletion of amino acids 42 to 47 and 66 to 71 also resulted in a loss of inhibitory activity but to a much lesser extent. Deletion analysis have thus indicated that the critical region of SDI-I polypeptide must lie between amino acids 42 to 71 , and fine studies implicate that the region between amino acids 48 to 65 are critical for the negative growth effects of the gene.

Claims 4 and 49 do not require making retroviral particles encoding amino acids 42-58 of SDI-1 capable of inhibiting cell proliferation in vivo.

Claim 50 is directed toward an isolated producer cell line transfected with a vector encoding amino acids 42-58 of SDI-1 capable of inhibiting cell proliferation.

Claim 50 does not require amino acids 42-58 of SDI-1 are capable of inhibiting cell proliferation *in vivo*.

Claim 53 is directed toward a method for introducing a DNA sequence encoding a polypeptide comprising amino acids 42-58 of human SDI-1 into a human cell in vitro, the method comprising infecting the human cell with a retroviral particle produced by the isolated producer cell line of claim 50, i.e. capable of inhibiting cell proliferation (see claim 50). Claim 53 does not require amino acids 42-58 of SDI-1 are capable of inhibiting cell proliferation *in vivo*.

Indefiniteness

I. Claims 1-4, 9-11, 13, 14, 19, 26, 27, 31, 33, 36-40, 43, 45, 48, 50 and 53-55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "upon infection of a target cell by said recombinant retroviral particle said SDI-1 coding sequence becomes operatively linked to said regulatory element or promoter and said regulatory element or promoter regulates expression of said SDI-1 coding sequence in said target cell" in claims 1, 13, 33, 39, 45, 50 as newly amended is indefinite similar to reasons of record. It is unclear if the phrase is describing a function of the retroviral particle made by the producer cell line, the retroviral vector, or the producer cell line. It is particularly unclear if the methods of claims 1 and 33 require a step of infecting a target cell or if the phrase is describing a functional limitation of the

retroviral particle. The ability of the recombinant retroviral particle to become operatively linked to the regulatory element or promoter as newly amended in claims 1, 13, 33, 39, 45 and 50 is clear in view of applicants' arguments. Applicants have not addressed this portion of the rejection.

The rejection regarding the phrase "a 5' LTR region of the structure U3-R-U5" (13, 39, 45, 50) has been withdrawn because the phrase has been deleted.

The rejection regarding the phrase "wherein into said deleted U3 region has been cloned a polylinker sequence into which a regulatory element or a promoter has been inserted" in claims 1, 13, 15, 39, 45 and 50 (and elsewhere) has been withdrawn in view of the amendment and applicants' arguments.

The rejection regarding the phrase "after infection of a target cell... ...said SDI-1 coding sequence in said target cell" in claim 1 and elsewhere has been withdrawn in part in view of the amendment and applicants' arguments.

The rejection regarding the phrase "said recombinant retroviral particle" in claim 13, (ii), has been withdrawn in view of the amendment.

Claim Rejections - 35 USC ' 103

The rejection of the claims under 35 U.S.C. 103(a) as being unpatentable over Miller (1989, Biotechniques, Vol. 7, pages 980-990) or Price (1987, PNAS, USA, Vol. 84, pages 156-160) in view of Nabel (US Patent 5,863,904, Jan 26, 1999) was withdrawn in the previous office action because the Miller, Price and Nabel did not teach

the retroviral vector with a deletion in the 3' LTR U3 region, wherein a promoter or regulatory element is inserted into the deletion as claimed.

The rejection of the claims under 35 U.S.C. 103(a) as being unpatentable over Gunzburg (WO 9607748, March 14, 1996) in view of Nabel (US Patent 5,863,904, Jan 26, 1999) was withdrawn in the previous office action because Gunzburg (published March 14, 1996) is not prior art in this application which has priority to Denmark patent application DK0740/95 filed June 27, 1995.

The claims remain free of the prior art because the prior art did not teach or suggest a retroviral vector with a deletion in the 3' LTR U3 region, wherein a promoter or regulatory element is inserted into the deletion as claimed.

Double Patenting

II. Claim 65 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 33. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). In this case, it is unclear how the phrase "and further wherein..." in claim 33 differentiates the method of claims 65 and 33. The structures and method step are otherwise identical.

Claim 66 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 39. When two claims in an application are duplicates or else are so close in

content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). In this case, it is unclear how the phrase "and further wherein..." in claim 33 differentiates the producer cell line of claims 66 and 39. The structure and function of the producer cell line in claim 66 is identical to the one in claim 39.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Claims 44 and 49 are allowed despite being objected to (see objections above).

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

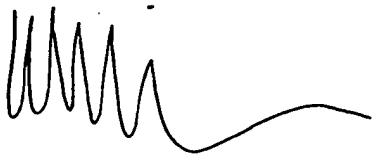
Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on 571-272-0735.

The official fax number for this Group is (571) 273-8300.

Michael C. Wilson



MICHAEL WILSON
PRIMARY EXAMINER